PATENT COOPERATION TREATY

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	icant's or agent's file form PCT/ISA/22			FOR FURTHER See paragraph 2 bel	
Inter	national application N	lo.	International filing date (Priority date (day/month/year) 07.11.2003
Inter	national Patent Class		both national classification	and IPC	
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	icant VARTIS AG	· .			
1.	This opinion co	ntains indicat	ions relating to the fol	llowing items:	
	Box No. I	Basis of the o	pinion		
	☐ Box No. II	Priority			
	☐ Box No. III			gard to novelty, inven	tive step and Industrial applicability
	☑ Box No. IV	Lack of unity	of invention	•	and the second s
	⊠ Box No. V	Reasoned sta applicability;	atement under Rule 43 <i>b.</i> citations and explanation	is.1(a)(i) with regard in a such start in a supporting such st	o novelty, inventive step or industrial atement
	☐ Box No. VI	Certain docur	ments cited	•	
	☐ Box No. VII	Certain defec	ts in the international ap	pplication	
	☐ Box No. VIII	Certain obser	vations on the internation	onal application	
2.	FURTHER ACT	ION			
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	and and the ID	EA a written re date of mailing	niv together where anni	ropriate with americi	e IPEA, the applicant is invited to nents, before the expiration of three on of 22 months from the priority date,
	For further optic	ons, see Form F	PCT/ISA/220.		
3.	For further deta	ils, see notes to	Form PCT/ISA/220.	•	
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Na	me and mailing addr	ess of the ISA:		Authorized Officer	
-	Europear D-80298	n Patent Office Munich		Novak-Giese,	
-	Tel. +49 Fax: +49	89 2399 - 0 Tx: 5 89 2399 - 4465	23656 epmu d	Telephone No. +4	9 89 2399-8930
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International application No. PCT/EP2004/012572

	Box		
	the la	ingu	rd to the language , this opinion has been established on the basis of the international application in age in which it was filed, unless otherwise indicated under this item.
	l (angu Junde	or Rules 12.3 and 23.1(b)).
2.	With nece	rega ssar	rd to any nucleotide and/or amino acid sequence disclosed in the international application and y to the claimed invention, this opinion has been established on the basis of:
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] fi	urnished subsequently to this Authority for the purposes of search.
3	. 🗆	has	ddition, in the case that more than one version or copy of a sequence listing and/or table relating thereto been filed or furnished, the required statements that the information in the subsequent or additional es is identical to that in the application as filed or does not go beyond the application as filed, as — ropriate, were furnished.
4	. Add	lition	al comments:

International application No. PCT/EP2004/012572

Box No. IV					
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		n establ	ished in re	espect of the following parts of the international applic	ation:
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	ts relating to claims Nos	. 18-42		· .	
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1. Statemen					
Novelty (N	N)	Yes: No:	Claims Claims	27,39 18-26, 28-38,40-42	
Inventive	step (IS)	Yes: No:	Claims Claims	18-42	
Industrial	applicability (IA)	Yes: No:	Claims Claims	18-42	
2. Citations	and explanations				

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: Database Geneseq, 28 March 2003, "Human fibroblast growth factor 23 polypeptide." Database accession no. ABP58110
- D2: WO 02/088358 A (GENEPROT INC.) 7 November 2002
- D3: WO 01/66596 A2 (CHIRON CORP.) 13 September 2002
- D4: Jonsson K. et al., "Fibroblast growth factor 23 in oncogenic osteomalacia and X-linked hypophosphatemia", N. Engl. J. Med., **vol. 348**, April 24 2003, pages 1656-1663.
- 1. Novelty
- 1.1. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 18-26, 28-38 and 40-42 is not new in the sense of Article 33(2) PCT.
- 1.2. The document D1 discloses (the references in parentheses applying to this document): the protein sequence derived from human fibroblast growth factor 23 (FGF23), comprising amino acids 177-251 of full length FGF23. also encompassed are methods to produce said polypeptide, uses of the polypeptide and its agonists and antagonists for treating disorders related to FGF23.
- 1.3. Please note that D2-D4 relate also to FGF23, respectively variants thereof, in the context of diseases linked to mutations or aberrations of this gene. Also encompassed by said documents are diagnostic and therapeutic agents related to the polynucleotides and proteins, including probes and antibodies (see e.g. abstract of D3).
 - As such, also these documents are prejudicial to the novelty of claims 18-26, 28-38 and 40-42; this is especially true since the claims encompass not further defined fragments of FGF23, thereto hybridizing molecules and bioactive polypeptides having 50% identity.

- 2. Inventive Step
- 2.1. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 27 and 39 does not involve an inventive step in the sense of Article 33(3) PCT.

The document D1 is regarded as being the closest prior art to the subject-matter of claims 27 and 39.

The subject-matter of claims 27 and 39 therefore differs from this known FGF23 fragment in that D1 discloses a fragment comprising amino acids 177-251 of the C-terminus.

The problem to be solved by the present invention may therefore be regarded as the provision of an additional C-terminal FGF23 fragment.

The solution proposed in claim 27, respectively 39 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons.

The provision of an alternative (fragment) requires an advantageous or surprising feature in order to justify an inventive step.

However, no such advantage can be derived from the description and/or in the examples of the patent application.

Both fragments appear to be used in the same medical applications, and no experimental support has been found in the application that the fragment of claims 27 and 39 display any superior quality to the fragments known in the art.

PATENT COOPERATION TREATY

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nter	national application N	lo.	International filing date (day/month/year)	Priority date (day/month/year)
	T/EP2004/012572		05.11.2004		07.11.2003
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	2N15/19				
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10	VARTIS AG				
1.	This opinion co	ntains indicati	ons relating to the fol	lowing items:	
	⊠ Box No. I	Basis of the or	pinion		
	☐ Box No. II	Priority			
	☐ Box No. III	Non-establish	most of opinion with rea	t to a seculity a forcement	and inductrial applicability
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Novak-Giese, S

Telephone No. +49 89 2399-8930



International application No. PCT/EP2004/012572

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International application No. PCT/EP2004/012572

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PCT/EP2004/012572

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: Database Geneseq, 28 March 2003, "Human fibroblast growth factor 23 polypeptide." Database accession no. ABP58110
- D2: WO 02/088358 A (GENEPROT INC.) 7 November 2002
- D3: WO 01/66596 A2 (CHIRON CORP.) 13 September 2002
- D4: Jonsson K. et al., "Fibroblast growth factor 23 in oncogenic osteomalacia and X-linked hypophosphatemia", N. Engl. J. Med., **vol. 348**, April 24 2003, pages 1656-1663.
- 1. Novelty
- 1.1. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 18-26, 28-38 and 40-42 is not new in the sense of Article 33(2) PCT.
- 1.2. The document D1 discloses (the references in parentheses applying to this document): the protein sequence derived from human fibroblast growth factor 23 (FGF23), comprising amino acids 177-251 of full length FGF23. also encompassed are methods to produce said polypeptide, uses of the polypeptide and its agonists and antagonists for treating disorders related to FGF23.
- 1.3. Please note that D2-D4 relate also to FGF23, respectively variants thereof, in the context of diseases linked to mutations or aberrations of this gene. Also encompassed by said documents are diagnostic and therapeutic agents related to the polynucleotides and proteins, including probes and antibodies (see e.g. abstract of D3).
 - As such, also these documents are prejudicial to the novelty of claims 18-26, 28-38 and 40-42; this is especially true since the claims encompass not further defined fragments of FGF23, thereto hybridizing molecules and bioactive polypeptides having 50% identity.

- 2. Inventive Step
- 2.1. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 27 and 39 does not involve an inventive step in the sense of Article 33(3) PCT.

The document D1 is regarded as being the closest prior art to the subject-matter of claims 27 and 39.

The subject-matter of claims 27 and 39 therefore differs from this known FGF23 fragment in that D1 discloses a fragment comprising amino acids 177-251 of the C-terminus.

The problem to be solved by the present invention may therefore be regarded as the provision of an additional C-terminal FGF23 fragment.

The solution proposed in claim 27, respectively 39 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons.

The provision of an alternative (fragment) requires an advantageous or surprising feature in order to justify an inventive step.

However, no such advantage can be derived from the description and/or in the examples of the patent application.

Both fragments appear to be used in the same medical applications, and no experimental support has been found in the application that the fragment of claims 27 and 39 display any superior quality to the fragments known in the art.